

Tissue Banks as Research Platforms - A playground for virtual microscopy?



**S. Macher-Göppinger, E. Herpel,
P. Schirmacher**

Institute of Pathology
Tissue Bank of the NCT

University of Heidelberg & DKFZ Heidelberg



Tissue banks - Resource and Technology Research Platforms

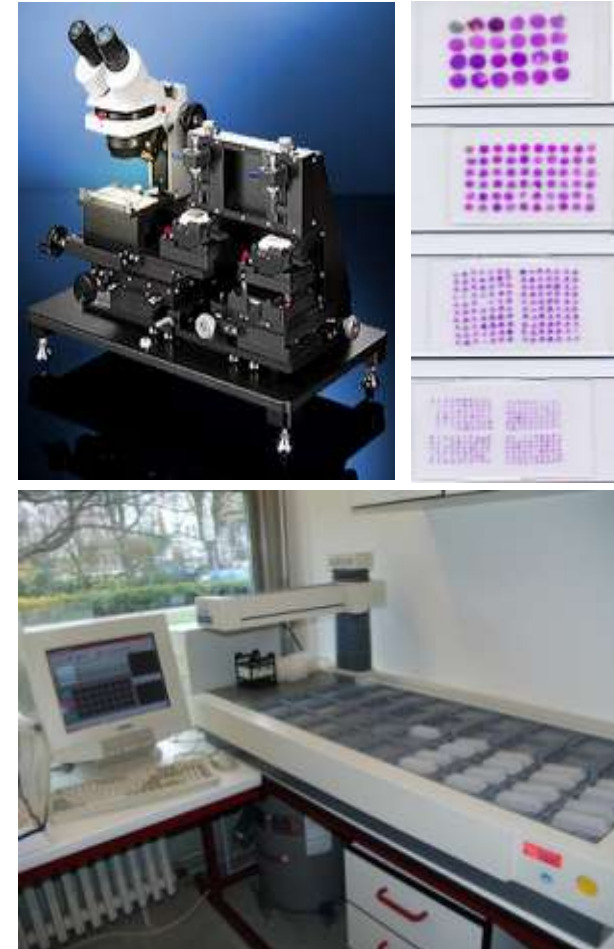
- Collection, storage, and distribution of tissues under standardized conditions
- **Composition of project related tissue collectives; link to clinical, histological, and follow-up data**
- **Specific derivatives**
- **Technology platform**
- **Project management**
- **Quality management**

Structural measures of NCT tissue bank

- Business order; standardized reviews (2005)
- Sustainability: section of NCT; basic budget (2005)
- Standard Operating Procedures (2006)
- Quality management; accreditation (2006-9)
- Complete legal/ethical framework (2005)
 - Comprehensive ethical vote
 - Standardized and comprehensive informed consent
 - Arrangements with funding organisations

Central Laboratory Tissue Bank

- Paraffin- and Frozen Sections
- H&E- and Special Stains
- Multi-Tissue-Arrays
- Immunohistology
- Registration und Handling of Frozen Tissues
- Paraffin Tissue Collectives
- Reference and Training



Multi-Tissue Arrays

- Breast (5x; n>500)
- Lung (3x; n>300)
- SCC Skin (n=176)
- HCC (n=230)
- RCC (n=932)
- Thymoma (n=112)
- Malignant Lymphoma (n=20)
- Colon Cancer (n=337)
- Colon Cancer (DACHS; n=1400)
- Colon Adenoma (n=54)
- Bladder Cancer (n=130)
- Pan-normal (n=120)
- Pan-Tumor (n=120)
- Pancreas (exocrine: n=400; endocrine: n=70))
- Small Bowel/Papilla (n=60)
- Prostate (n=275)
- Sarkoma (n=900, ongoing)

Standards

- Project related
- Linked with VM and IT
- Only Study Collectives
 - Clinical trials
 - Epidemiological Studies

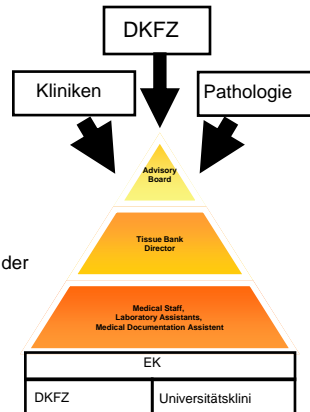
Structural

1. Structure
2. Regulations
3. Consent Forms
4. Reviews

1. Structure

- Non-profit
- Keine Gebühren (für Mitglieder)
- Funding durch NCT
- Ortsbezogen

Abb. 1: Organigramm der NCT-Gewebebank



2. Regulations

- Geschäftsordnung
- Ausformulierte und umgesetzte Standard Operating Procedures (SOPs)

3. Reviews

- Berichterstattung an Beirat der Gewebebank (2x/Jahr)
- Review durch NCT (jährlich)
- Externer Review (im Rahmen NCT-Begutachtung; alle 3 Jahre)
- Geplant: Akkreditierung

4. Consent Forms

- Ethisch-rechtliche Rahmenbedingungen
- Kompletter Review aller ethischen Belange durch Ethikkommission Heidelberg
- Standardisierter Patientenaufklärungsbogen
- Teil des Patientenaufnahmevertrages (zusätzlich)
- Kontrolle (stichpunkthaft) und Forschung über Patientenverfügung

Abb. 2: Standardisierte Patientenaufklärung



GSP

1. Tissue Quality
2. Project Management
3. Tracking

Tissue Quality

- SOPs für alle manuellen Prozeduren
- Gewebeausgangskontrolle und -beurteilung
- Übergabeprotokoll mit Gewebedaten
- Interne Projektdokumentation

Das Bild zeigt ein Übergabeprotokoll, das die Gewebedaten und die Übergabeprozessschritte dokumentiert.

Abb. 3: Übergabe-Protokoll

Project Management

- Standardisierter Projektantrag (Initiation)
- Projektreview durch Gewebebank (Machbarkeit, Ressourcenschonung, Projektbetreuung)
- Projektreview durch Board (bei ‚Fremdnutzung‘, Konfliktfällen)

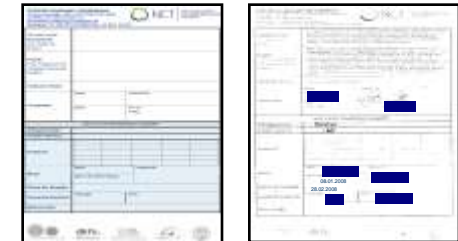


Abb. 4: Standardisierter Projektantrag

3. Tracking

- Automatischer Recall nach 90 and 180 Tagen (Qualität; Geweбенutzung) mit Dokumentation
- Forschung und Publikationen (geplant) über Projektergebnisse

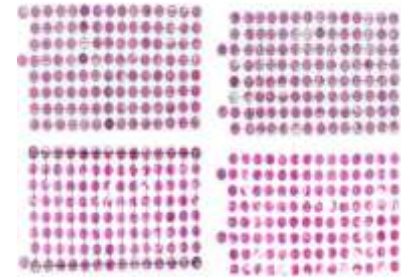

NCT | NATIONALES CENTRUM
 FÜR TUMORERKRANKUNGEN
 HEIDELBERG

NCT-Nr	GEWEBE	TUMOR VITAL (%)	TUMOR NEKROSE (%)	TUMOR STROMA (%)	DIAGNOSE/LOKALISATION/ANMERKUNG	
TUMOR:						
1	218	PLECA	50	7	50	stark differenziert, gering vaskularisiert, invasives Plattenepithelkarzinom (Zungenrund) (Zungenrund)
2	266	PLECA	70	1	30	stark differenziertes, schlecht vaskularisiertes Plattenepithelkarzinom (Zungenrund) mit metastatischen Cytokeratinherdungen
3	288	PLECA	70	10	20	stark differenziertes Plattenepithelkarzinom (Larynx)
4	300	PLECA	70	10	20	stark differenziertes Plattenepithelkarzinom (Tonsillen)
5	303	PLECA	60	10	30	stark differenziertes Plattenepithelkarzinom (Tonsillen)
6	329	PLECA	80	10	10	Malignes Melanom eines niedrig differenzierten Plattenepithelkarzinom (Tonsillen)
7	341	PLECA	30	30	40	niedrig differenziertes Plattenepithelkarzinom (Tonsillen)
8	351	PLECA	40	10	10	niedrig differenziertes Plattenepithelkarzinom (Tonsillen)
9	386	PLECA	60	5	35	stark differenziertes Plattenepithelkarzinom (Tonsillen)
10	420	PLECA	60	10	10	stark differenziertes Plattenepithelkarzinom (Tonsillen)
11	461	PLECA	40	10	50	Plattenepithelkarzinom der rechten Kehlkopf (Anatomie, Entzündung)
12	546	PLECA	70	10	20	stark differenziertes Plattenepithelkarzinom (Zungenrund) (Zungenrund)
13	562	PLECA	60	7	40	stark differenziertes Plattenepithelkarzinom des Kehlkopfes (Kehlkopf)
14	603	PLECA	90	7	10	stark differenziertes Plattenepithelkarzinom (Zungenrund)
15	680	PLECA	50	10	30	stark differenziertes Plattenepithelkarzinom (Larynx)
16	716	PLECA	40	10	50	stark differenziertes Plattenepithelkarzinom (Zungenrund)



Status NCT tissue bank

- Projects: 311 (1/2009)
- Completed projects: 307/311 (>98%)
- Multi-Tissue-Arrays: 30 (2)
- Frozen tissues: >10.000 (increasing; 2/3 retrospective)
- Access paraffin archive (>500.000)
- Service for large national/international trials (EPIC, DACHS)
- Positive 3y international review (2008)
- Accreditation (2009)



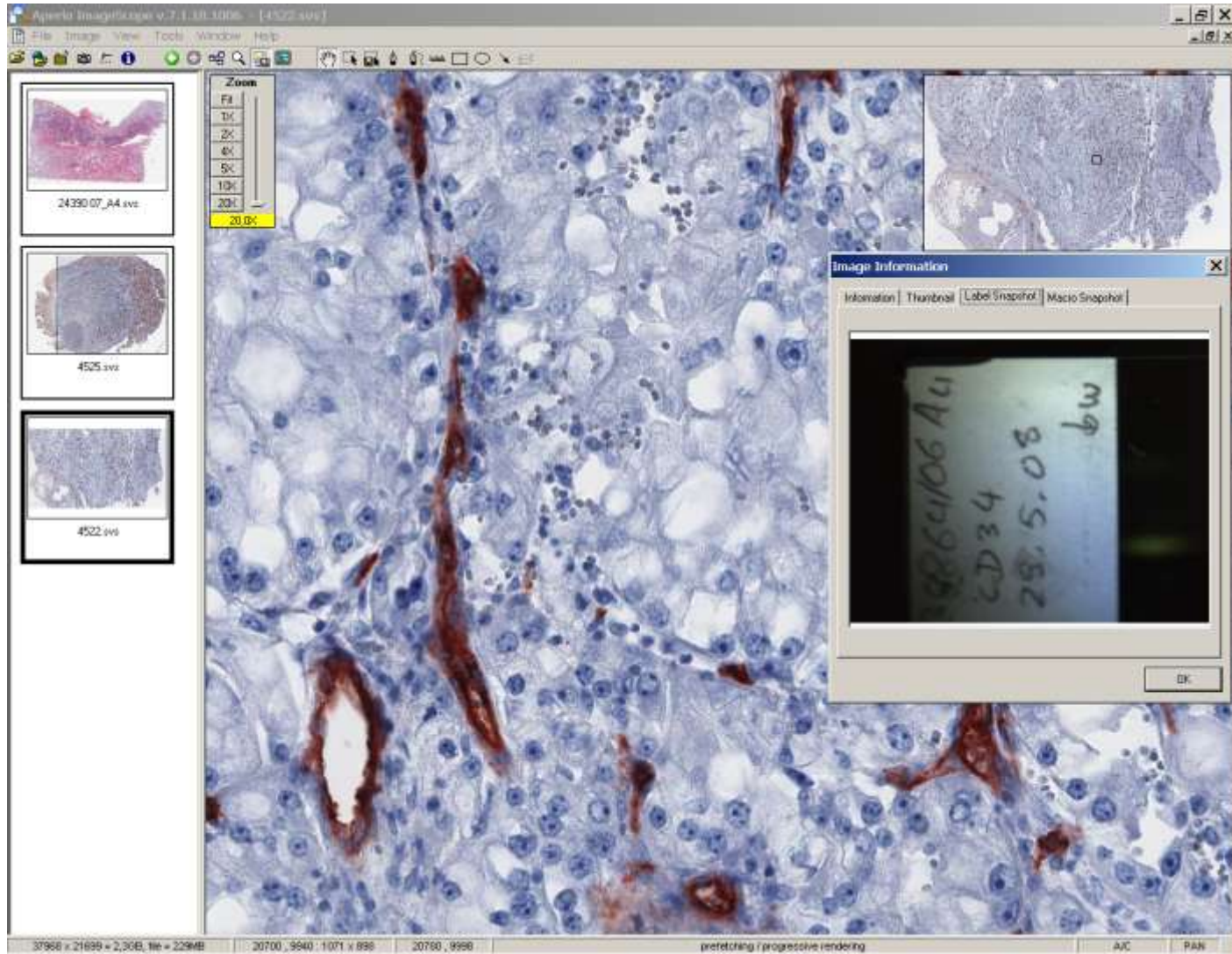
Virtual microscopy in Tissue Banking

- Documentation
 - Reference Slides
- Slide/Multi-Tissue-Arrays analyses
 - Data acquisition and storage
 - Data banks and correlative analysis/bioinformatics
- Project management/Core function
 - Management of decentral projects
 - Contributions to international projects

Why digitalize tissue bank reference slides / TMAs?

- Avoid quality loss
- Potential to copy
- Save resources (no repetitive sections)
- Independence from microscope access and slide location
- Simultaneous analyses
- Easy generation of figures (publications)

Slide information storage



Why annotate digitalized TMAs?

- Easy dot location
- Minimize evaluation mistakes
- Mark-ups
- Automated evaluation

Digital data acquisition and analysis

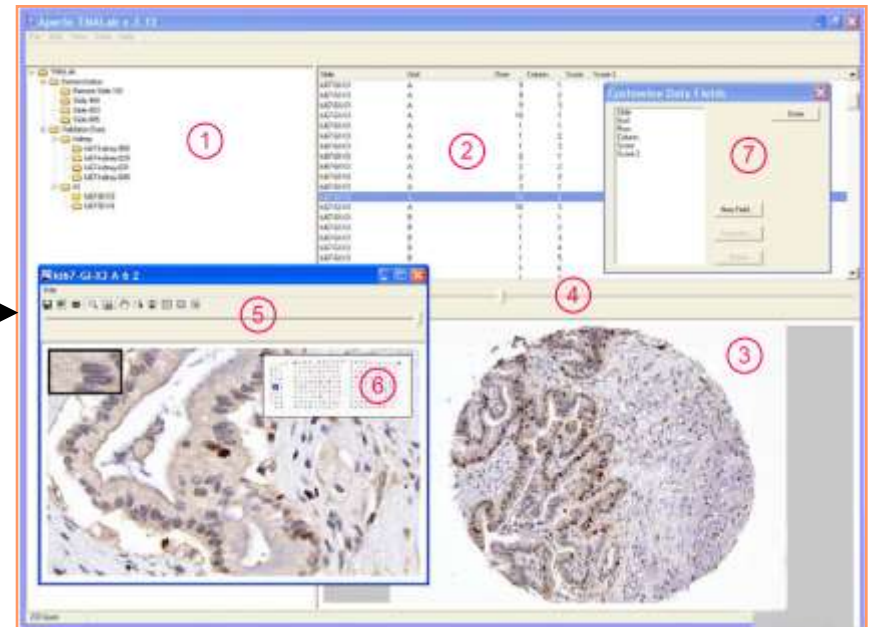
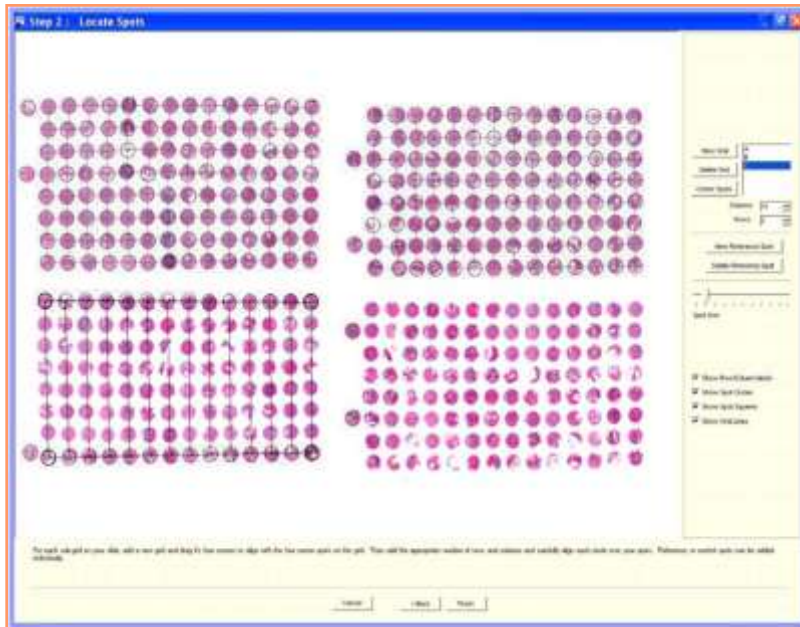
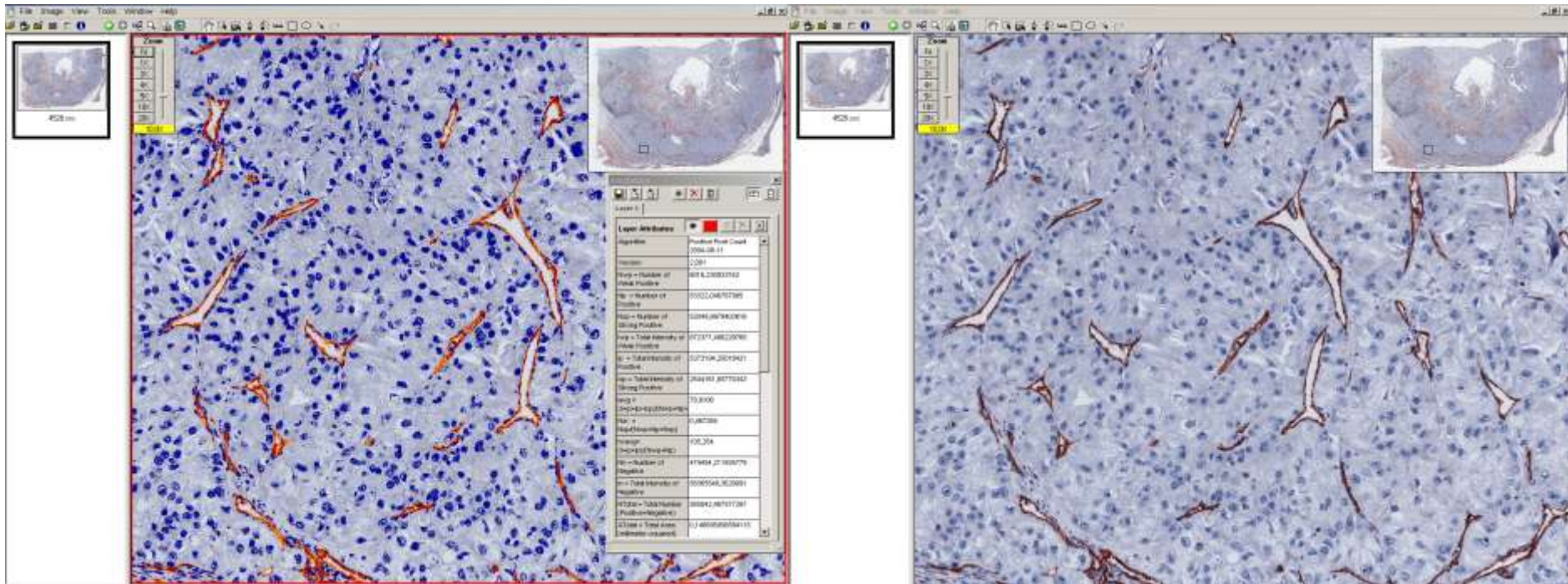
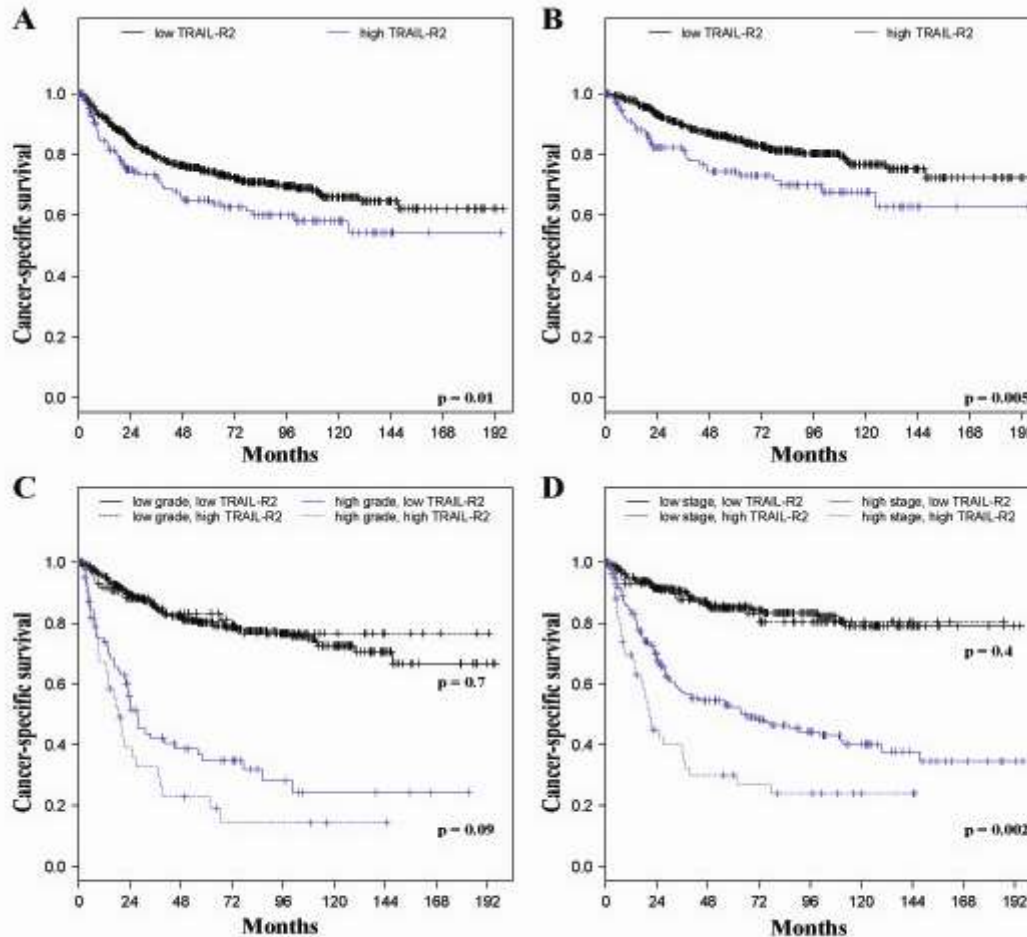


Image analysis

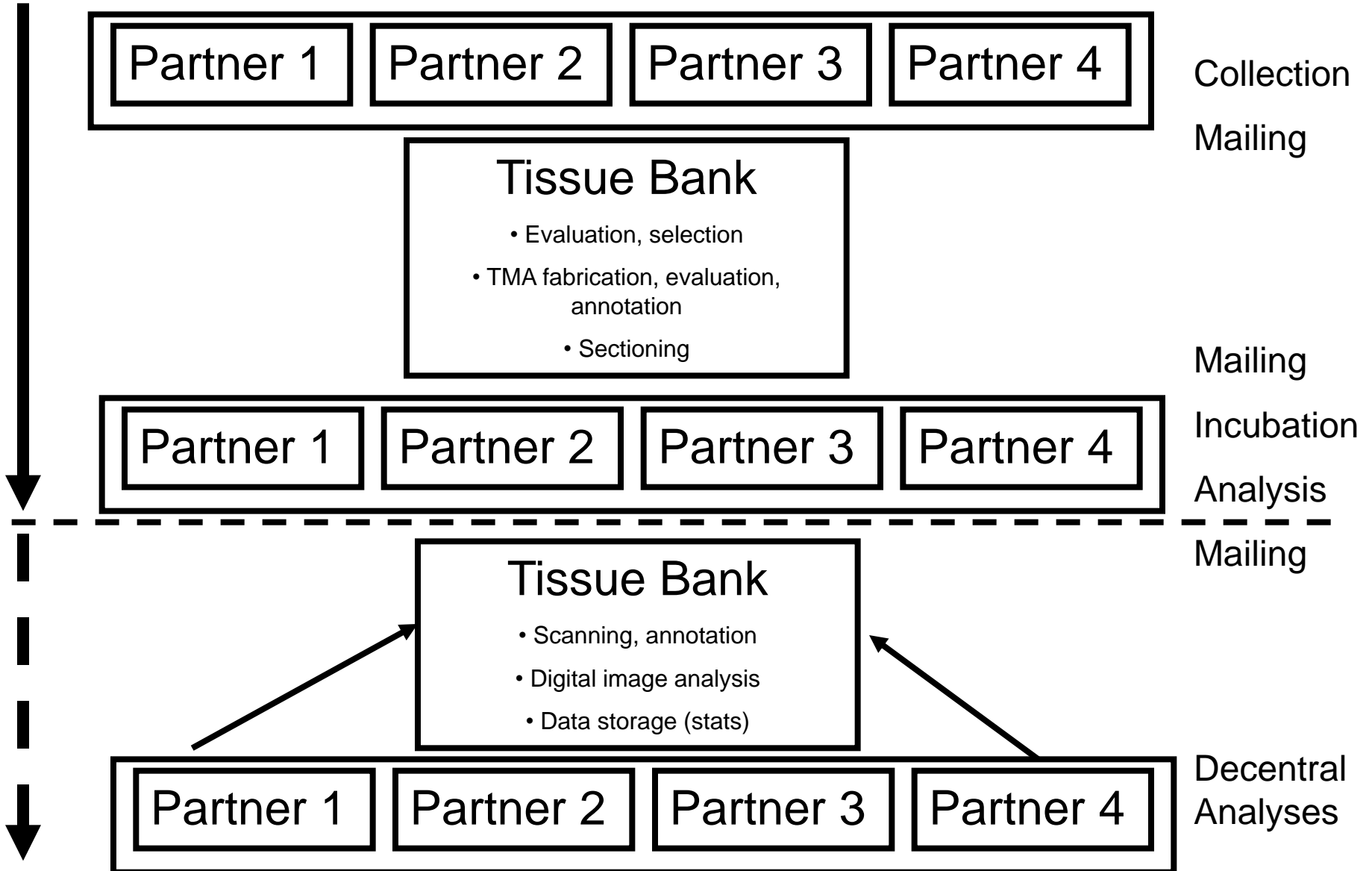


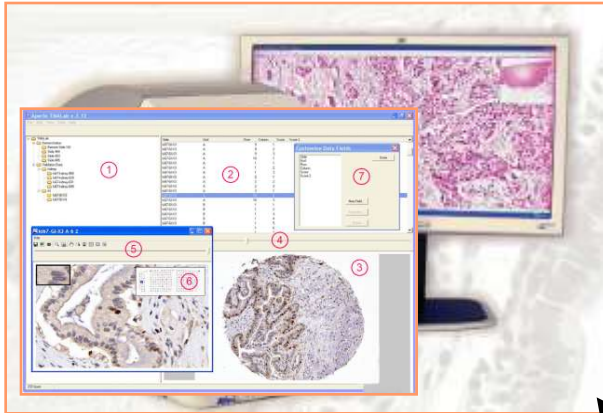
Correlative Data Analyses



Why generate central TMA databases?

- Improved data assembly
- Facilitates data archiving and transfer
- Facilitates statistical analyses and bioinformatics
- Supports decentral consortial projects

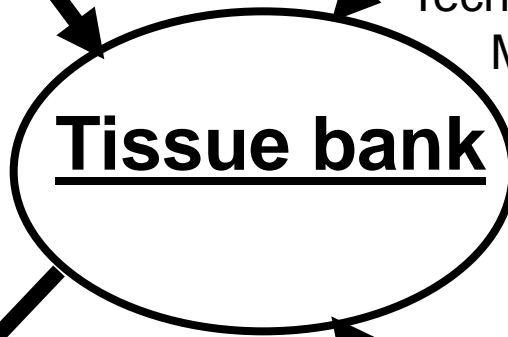




TMA-VM; Digital Image Analysis (Pathology)

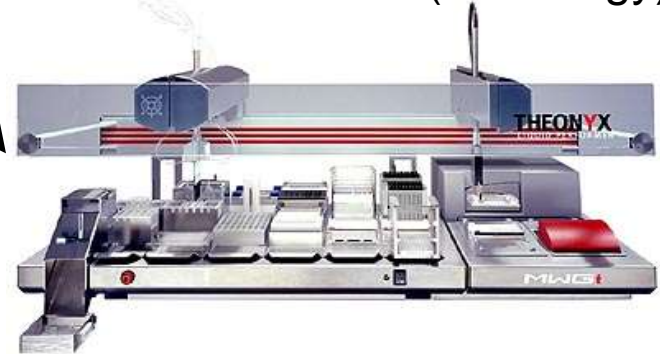


Tech Development/ Quantitative Marker-Analyses (TIGA)



Paraffin-Profiling, Laser-Microdissection (Pathology)

Bioinformatics



Conclusions

- VM is the ideal measure for slide reference in a tissue bank core
- VM is the ideal basis for digitalizing TMAs with subsequent annotation, image analysis, database generation, and subsequent statistical analyses and bioinformatics
- VM is an ideal measure to support decentral tissue based consortial projects
- VM may be a relevant mean to provide open access to primary tissue data and supplementary information in publications

Contributors

- Institute of Pathology, University Hospital
 - S. Macher-Göppinger
- Tissue Bank of the NCT Heidelberg
 - E. Herpel
 - B. Schreiber
 - B. Walther
- TIGA Center Heidelberg
 - N. Grabe